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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|-----------------|-------------|----------------------|---------------------|
|-----------------|-------------|----------------------|---------------------|

09/551,380 04/18/00 CHANG

D MLY-5

EXAMINER

HM12/1024

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ART UNIT

PAPER NUMBER

1652

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DATE MAILED:

10/24/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.
09/551,380

Applicant(s)
Chang et al.

Examiner
Christian L. Fronda

Art Unit
1652



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above, claim(s) 8-24 and 27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7, 25, and 26 is/are rejected.
- 7) ☒ Claim(s) 6 is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 9
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

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DETAILED ACTION

Election/Restriction

1. Applicants' election with traverse of Group I, claims 1-7, 25, and 26, in the **RESPONSE TO ELECTION/RESTRICTION REQUIREMENT** dated August 20, 2001 (Paper No. 7) is acknowledged. The traversal is on the ground(s) that the written information for the restriction requirement is not adequate to explain the various groupings which have the same class and/or subclass, the polynucleotide of Group II and polypeptide of Group I are "sufficiently interlinked that different literature searches are not required", and that the species requirement for claim 6 is inappropriate.

This is not found persuasive because although Groups III and IV, V and VI, VII and VIII, and IX-XI share the same class and subclass, each of the processes are distinct both physically and functionally; require different process steps, reagents, and parameters; and have different purposes. The polypeptide of Group I and the polynucleotide of Group II are distinct chemical substances with different chemical properties that require separate searches in the patent literature and the non-patent literature. The species requirement for claim 6 is proper since each of the proteins are distinct entities that have different structures/sequences and chemical properties.

The requirement is still deemed proper and is therefore made FINAL.

Claims 8-24 and 27; MD9, D4, D7, D8, E2, E3-1, E3-5, E3-9, E3-12, E4-a, E4-g, E4-j, E4-o, E4-p, BFP, CFP, YFP, and DsRed; and SEQ ID NOs: 7-13 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

2. Claims 1-7, 25, and 26 and the species of D9 and SEQ ID NO: 4 are under consideration in this Office Action.

Claim Objections

3. Claims 5-7 are objected to because of the following informalities: Claims 5-7 recite non-elected subject matter, specifically, MD9, D4, D7, D8, E2, E3-1, E3-5, E3-9, E3-12, E4-a, E4-g, E4-j, E4-o, E4-p, BFP, CFP, YFP, and DsRed and SEQ ID NOs: 7-13. Applicant is required to cancel the claims or amend the claims to recite the elected subject matter which is D9 and SEQ ID NO: 4.

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Claim Rejections - 35 U.S.C. § 112, 1st Paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 3-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are directed toward all fluorescent proteins having a protease cleavage site “incorporated in the loop structure joining any pair of adjacent β -sheets”. The claimed invention requires the crystal structure of any fluorescent protein in order to identify, determine the number, and position of any β -sheet structure. The specification does not provide a written description of any crystal structure of any fluorescent protein having a protease cleavage site “incorporated in the loop structure joining any pair of adjacent β -sheets”. There is no disclosure on the specific crystallization conditions to make any crystal structure of any fluorescent protein having a protease cleavage site “incorporated in the loop structure joining any pair of adjacent β -sheets” which would be suitable for x-ray diffraction. The specification only provides the crystal structure of green fluorescent protein (GFP) on page 10, lines 6-9. Given this lack of written description of any fluorescent protein having a protease cleavage site “incorporated in the loop structure joining any pair of adjacent β -sheets” as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

6. Claims 3-5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a green fluorescent protein (GFP) having a protease cleavage site incorporated in the loop structure between β -sheet numbers 9 and 10, 5 and 6, and 8 and 9 based on the crystal structure of GFP described in the specification on page 10, lines 6-9; does not reasonably provide enablement for any fluorescent protein having a protease cleavage site “incorporated in the loop structure joining any pair of adjacent β -sheets”. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *re Wands* [858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)]. The *Wands* factors

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are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses any fluorescent protein having a protease cleavage site “incorporated in the loop structure joining any pair of adjacent β -sheets”. However, the specification provides guidance and examples for a green fluorescent protein (GFP) having a protease cleavage site incorporated in the loop structure between β -sheet numbers 9 and 10, 5 and 6, and 8 and 9 based on the crystal structure of GFP described in the specification on page 10, lines 6-9. The claimed invention requires the crystal structure of any fluorescent protein in order to identify, determine the number, and position of any β -sheet structure. While molecular biological techniques and several crystallization methods for proteins are known in the prior art and the skill of the artisan are well developed, knowledge regarding the specific fluorescent protein and how to obtain a suitable crystal for structure determination by X-ray is lacking. Thus, searching for any fluorescent protein and for crystallization conditions to obtain an adequate crystal of any fluorescent protein for structure determination by x-ray diffraction method is well outside the realm of routine experimentation and predictability in the art of success is extremely low, see Branden et al. page 271.

The conditions of crystallization is highly dependent on the fluorescent protein itself and any minor change in the amino acid sequence may require search for new crystallization conditions. The amount of experimentation to identify the specific fluorescent protein and conditions to grow a single crystal suitable for structure determination in order to identify, determine the number, and position of any β -sheet structure is enormous. Since routine experimentation in the art does not include screening for vast numbers of fluorescent proteins and crystallization conditions where the expectation of obtaining the desired crystal is unpredictable, the Examiner finds that one skilled in the art would require additional guidance, such as information regarding the exact fluorescent protein to be crystallized and the conditions under which the fluorescent protein would crystallize and produce an adequate crystal for structural determination by X-ray. Without such a guidance, the experimentation left to those skilled in the art is undue.

Claim Rejections - 35 U.S.C. § 112, 2nd Paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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8. Claims 3, 4, and 5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 3, the phrase "cleavage site incorporated in the loop structure joining any pair of adjacent β -sheets" renders the claim indefinite because the specific structure/amino acid sequence of the "modified fluorescent protein" and the "loop structure joining any pair of adjacent β -sheets" are not known and one of skill in the art cannot determine the metes and bounds of the claimed invention.

In claim 4, the phrase "selected from the group consisting of β -sheets numbers 9 and 10, 5 and 6, and 8 and 9" renders the claim indefinite because the specific structure/amino acid sequence and position of the " β -sheets" are not known and one of skill in the art cannot determine the metes and bounds of the claimed invention.

In claim 5, the recitation of the protein name D9 renders the claim indefinite because the specific structure/amino acid sequence is not recited in the claim. For examination purposes, it is assumed D9 consists of the amino acid sequence of SEQ ID NO: 41.

Claim Rejections - 35 U.S.C. § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1, 2, 7, 25, and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Xu et al.

Xu et al. teach a green fluorescent protein (GFP) that is linked by an 18 amino acid peptide containing the caspase-3 (CPP32) cleavage site, DEVD, to blue fluorescent protein (BFP), wherein cleavage at the cleavage site results in alteration of at least one of the emission and excitation spectra (see entire publication and Figure 2). Thus, the reference teachings anticipate the claimed invention.


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Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L. Fronda whose telephone number is (703)305-1252. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703)308-3804. The fax phone number for this Group is (703)308-0294. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703)308-0196.

CLF


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